

WHAT IS CLAIMED IS:

1 1. A composition comprising a biologically active compound and a
2 transport moiety, wherein the transport moiety comprises a structure selected from the group
3 consisting of (ZYZ)_nZ, (ZY)_nZ, (ZYY)_nZ and (ZYYY)_nZ, wherein each Z is L-arginine or D-
4 arginine, and each Y is independently an amino acid that does not comprise an amidino or
5 guanidino moiety, and wherein n is an integer of from 2 to 10.

1 2. The composition according to claim 1, wherein each Y is
2 independently selected from the group consisting of alanine, cysteine, aspartic acid, glutamic
3 acid, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine,
4 proline, glutamine, serine, threonine, valine, tryptophan, hydroxyproline, tyrosine, γ-amino
5 butyric acid, β-alanine, sarcosine and ε-amino caproic acid.

1 3. The composition according to claim 1, wherein the transport moiety
2 comprises the structure (ZYZ)_nZ, and wherein n is an integer ranging from 2 to 5.

1 4. The composition according to claim 1, wherein the transport moiety
2 comprises the structure (ZY)_nZ, and wherein n is an integer ranging from 4 to 10.

1 5. The composition according to claim 1, wherein the transport moiety
2 comprises the structure (ZYY)_nZ, and wherein n is an integer ranging from 4 to 10.

1 6. The composition according to claim 1, wherein the transport moiety
2 comprises the structure (ZYYY)_nZ, and wherein n is an integer ranging from 4 to 10.

1 7. The composition according to claim 1, wherein the transport moiety is
2 attached to the biologically active compound by a linking moiety to form a conjugate.

1 8. The composition according to claim 1, wherein Y is a gene-encoded
2 amino acid.

1 9. The composition according to claim 1, wherein Y is an amino acid
2 other than a gene-encoded amino acid.

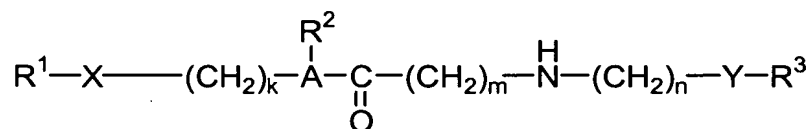
1 10. The composition according to claim 3, wherein each Y is
2 independently selected from the group consisting of glycine, γ-amino butyric acid, β-alanine
3 and ε-amino caproic acid, and n is 3 or 4.

11. The composition according to claim 4, wherein each Y is independently selected from the group consisting of glycine, γ -amino butyric acid, β -alanine and ϵ -amino caproic acid, and n is 6, 7 or 8.

12. The composition according to claim 5, wherein each Y is independently selected from the group consisting of glycine, γ -amino butyric acid, β -alanine and ϵ -amino caproic acid, and n is 6, 7 or 8.

13. The composition according to claim 6, wherein each Y is independently selected from the group consisting of glycine, γ -amino butyric acid, β -alanine and ϵ -amino caproic acid, and n is 6, 7 or 8.

14. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

R^1 is the biologically active compound ;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R^1 and R^3 ;

Y is a linkage between a functional group on the transport moiety and a functional group on the linker between R^1 and R^3 ;

A is N or CH;

R^2 is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

R^3 is a transport moiety;

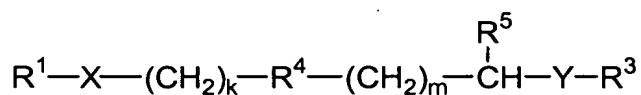
k and m are independently either 1 or 2; and

n is an integer of from 1 to 10.

15. The composition according to claim 14, wherein each of X and Y is independently selected from the group consisting of $-C(O)O-$, $-C(O)NH-$, $-OC(O)NH-$, $-S-S-$, $-C(S)O-$, $-C(S)NH-$, $-NHC(O)NH-$, $-SO_2NH-$, $-SONH-$, phosphate, phosphonate and phosphinate.

16. The composition according to claim 14, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and -NHC(O)NH-.

17. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

R¹ is the biologically active compound ;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R¹ and R³;

Y is a linkage between a functional group on the transport moiety and a functional group on the linker between R¹ and R³;

R³ is a transport moiety;

R⁴ is S, O, NR⁶ or CR⁷R⁸;

R⁵ is OH, SH or NHR⁶;

R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

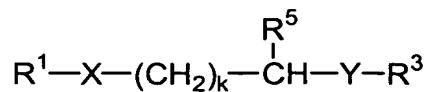
R⁷ and R⁸ are independently hydrogen, alkyl or arylalkyl; and

k and m are independently either 1 or 2.

18. The composition according to claim 17, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO₂NH-, -SONH-, phosphate, phosphonate and phosphinate.

19. The composition according to claim 17, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and -NHC(O)NH-.

20. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

R¹ is the biologically active compound;

X is a linkage between a functional group on the biologically active compound
and a functional group on the linker between R¹ and R³;

Y is a linkage between a functional group on the transport moiety and a functional
group on the linker between R¹ and R³;

R³ is the transport moiety;

R⁵ is H, OH, SH or NHR⁶;

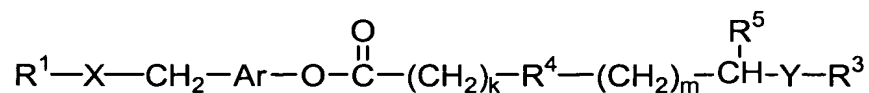
R⁶ is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl; and

k is 1 or 2.

21. The composition according to claim 20, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO₂NH-, -SONH-, phosphate, phosphonate and phosphinate.

22. The composition according to claim 20, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and -NHC(O)NH-.

23. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

R¹ is the biologically active compound;

X is a linkage between a functional group on the biologically active compound
and a functional group on the linker between R¹ and R³;

Y is a linkage between a functional group on the transport moiety and a functional
group on the linker between R¹ and R³;

Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen
substituents are either *ortho* or *para* to one another;

R³ is the transport moiety;

R⁴ is S, O, NR⁶ or CR⁷R⁸;

R⁵ is H, OH, SH, CONHR⁶ or NHR⁶;

15 R^6 is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;
16 R^7 and R^8 are independently hydrogen or alkyl; and,
17 k and m are independently either 1 or 2.

1 **24.** The composition according to claim 23, wherein each of X and Y is
2 independently selected from the group consisting of $-C(O)O-$, $-C(O)NH-$, $-OC(O)NH-$, $-S-S-$,
3 $-C(S)O-$, $-C(S)NH-$, $-NHC(O)NH-$, $-SO_2NH-$, $-SONH-$, phosphate, phosphonate and
4 phosphinate.

1 **25.** The composition according to claim 23, wherein each of X and Y is
2 independently selected from the group consisting of $-C(O)O-$, $-C(O)NH-$, $-OC(O)NH-$ and
3 $-NHC(O)NH-$.

1 **26.** The composition according to claim 12, wherein A is N, R^2 is benzyl,
2 k, m and n are 1, and X is $-C(O)O-$.

1 **27.** The composition according to claim 13, wherein R^4 is S, R^5 is NHR^6 ,
2 R^6 is hydrogen, methyl, allyl, butyl or phenyl, k and m are 1 and X is $-C(O)O-$.

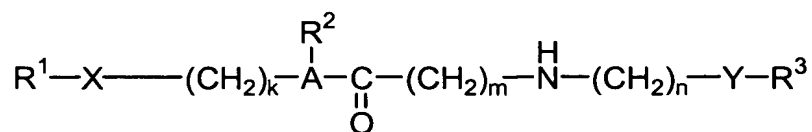
1 **28.** The composition according to claim 14, wherein R^5 is NHR^6 , R^6 is
2 hydrogen, methyl, allyl, butyl or phenyl, k is 2 and X is $-C(O)O-$.

1 **29.** The composition according to claim 15, wherein Ar is an unsubstituted
2 aryl group, R^4 is S, R^5 is NHR^6 , R^6 is hydrogen, methyl, allyl, butyl or phenyl, k and m are 1
3 and X is $-C(O)O-$.

1 **30.** A method for increasing the transport of a biologically active
2 compound across a biological membrane comprising:
3 administering a composition comprising a biologically active compound and a
4 transport moiety, wherein the transport compound comprises a structure selected from the
5 group consisting of $(YZ)_nZ$, $(ZY)_nZ$, $(ZYY)_nZ$ and $(ZYYY)_nZ$, wherein Z is L-arginine or
6 D-arginine, and wherein Y is an amino acid that does not comprise an amidino or guanidino
7 moiety, and wherein n is an integer ranging from 2 to 10,
8 wherein transport of the biologically active compound across the biological
9 membrane is increased relative to transport of the biologically active compound in the
10 absence of said transport moiety.

11
1 31. The method according to claim 20, wherein the biologically active
2 compound is attached to the transport moiety by a linking moiety to form a conjugate.

1 32. The method of claim 21, wherein the conjugate has the following
2 structure:



3
4 wherein:

5 R^1 is the biologically active compound ;

6 X is a linkage between a functional group on the biologically active compound
7 and a functional group on the linker between R^1 and R^3 ;

8 Y is a linkage between a functional group on the transport moiety and a functional
9 group on the linker between R^1 and R^3 ;

10 A is N or CH;

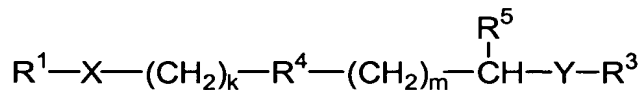
11 R^2 is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

12 R^3 is a transport moiety;

13 k and m are independently either 1 or 2; and

14 n is an integer of from 1 to 10.

1 33. The method of claim 21, wherein the conjugate has the following
2 structure:



3
4 wherein:

5 R^1 is the biologically active compound ;

6 X is a linkage between a functional group on the biologically active compound
7 and a functional group on the linker between R^1 and R^3 ;

8 Y is a linkage between a functional group on the transport moiety and a functional
9 group on the linker between R^1 and R^3 ;

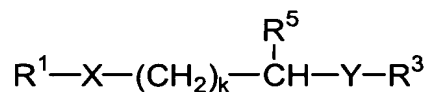
10 R^3 is a transport moiety;

11 R^4 is S, O, NR^6 or CR^7R^8 ;

12 R^5 is OH, SH or NHR^6 ;

R^6 is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;
 R^7 and R^8 are independently hydrogen, alkyl or arylalkyl; and
 k and m are independently either 1 or 2.

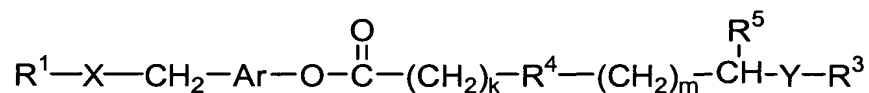
34. The method of claim 21, wherein the conjugate has the following structure:



wherein:

R^1 is the biologically active compound;
 X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R^1 and R^3 ;
 Y is a linkage between a functional group on the transport moiety and a functional group on the linker between R^1 and R^3 ;
 R^3 is the transport moiety;
 R^5 is H, OH, SH or NHR^6 ;
 R^6 is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl; and
 k is 1 or 2.

35. The method of claim 21, wherein the conjugate is of the following structure:



wherein:

R^1 is the biologically active compound;
 X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R^1 and R^3 ;
 Y is a linkage between a functional group on the transport moiety and a functional group on the linker between R^1 and R^3 ;
 Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen substituents are either *ortho* or *para* to one another;
 R^3 is the transport moiety;
 R^4 is S, O, NR^6 or CR^7R^8 ;
 R^5 is H, OH, SH, $CONHR^6$ or NHR^6 ;

- 15 R^6 is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;
16 R^7 and R^8 are independently hydrogen or alkyl; and,
17 k and m are independently either 1 or 2.

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